Drug & Poison Information Center—Faculty of Pharmacy—Tanta University

Drug & Poison Information Bulletin

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Synbiotics for Sepsis Prophylaxis in Infants

Sepsis is a major cause of neonatal morbidity and mortality. It is characterized by systemic inflammation and circulatory compromise initiated by an infection. No efficient means of prevention is currently available. Breastfeeding and applying antiseptics to the umbilical stump are two interventions that may be helpful as prophylaxis.

But, when neonatal sepsis is suspected, treatment should be initiated immediately because of the neonate's relative immunosuppression. Antibiotics should be used as soon as diagnostic tests are performed.

Unfortunately, antimicrobial resistance is increasing by an amazing rate worldwide. Using a probiotic in prevention or in combination with other therapies is advantageous as concerns deepen about antibiotic resistance.

Large study in rural India was conducted in 149 randomly chosen villages in Odisha state including 4,556 births on a randomized, double-blind, and placebo-controlled design. Newborns received the oral synbiotic preparation (*Lactobacillus plantarum* plus fructooligosaccharide) beginning on day two to four of life and then each day for a total of seven days.

The babies were monitored for 60 days. Synbiotics are combinations of probiotics with a prebiotic, the latter added to promote growth and sustain colonization of the probiotic strain.

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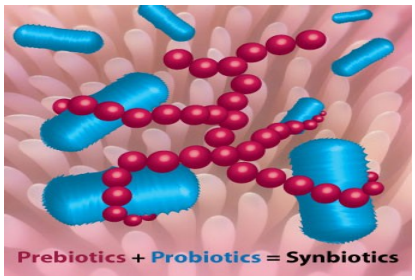
The group that received the synbiotic combination had a significant (40%) reduction (risk ratio, 0.60; 95% confidence interval, 0.48 - 0.74) in the primary combined outcome of death and sepsis compared with the placebo group (5.4% vs 9%, respectively). That was twice the 20% risk reduction expected, which led the data safety and monitoring board to stop the trial early. Deaths were rare: four in the placebo group and six in the synbiotic group.



In addition, the researchers found substantial reductions in all three components of sepsis they studied which include culture-positive sepsis, culture-negative sepsis, and lower respiratory tract infections.

The preparation was well tolerated, and gastrointestinal events were low with only six cases of abdominal distention (five in the placebo group; one in the treatment group) occurred.

Study limitations include that researchers did not enroll premature (less than 35 weeks of gestation) or low birth weight (less than 2000 g) babies, groups that have a higher risk of dying from sepsis. They also excluded 2506 infants (of 7089 births in the study region) who had major causes of morbidity and mortality in the early neonatal period.

Further studies would be needed to determine whether these results would extend to all at-risk infants in developing countries.

References:

⇒ ***Panigrahi P, Parida S, Nanda NC, et al. A randomized synbiotic trial to prevent sepsis among infants in rural India. Nature. 2017 Aug 24;548(7668):407-412.***

⇒ ***Frellick M. Probiotic Mix Fed to Indian Infants Cuts Newborn Sepsis Risk by 40%: http://www.medscape.com/viewarticle/884455. Accessed August 2017.***

By: Bassant Maher, B.Sc.

Modifications to Vancomycin Reduce Resistance

Scientists have discovered new peripheral modifications to the powerful antibiotic vancomycin that could eliminate the threat of antibiotic-resistant infections in a newly published study.

Previously, the researchers have reported two of the three modifications. The first is a modification of the cell wall binding pocket to directly overcome the molecular basis of vancomycin resistance. The second modification is the introduction of a new chemical group (quaternary ammonium salt) to C-terminal. This modification induces cell wall permeability and complements vancomycin's inhibition of cell wall synthesis, and is reported to provide enhancements in antimicrobial potency (200-fold) against *Vancomycin-Resistant Enterococci* (VRE).

In the new study, a third and new peripheral modification that also interferes with bacterial cell walls, but via a different mechanism. All the modifications combined together produce a 1000-fold increase in activity. To date, the modified antibiotic has been tested against resistant bacteria in the laboratory, where it was shown to be at least 25,000 times more potent against VRE and Vancomycin-Resistant Staphylococcus aureus. Furthermore, neither strain of bacteria acquired resistance even after 50 rounds of testing with the modified agent.

Currently, the development of new synthetic antibiotic molecule is a 30-step process, which impedes commercial production. Therefore, researchers are focused on simplifying the process and reducing its cost. The researchers hope that the modified vancomycin be clinically available within 5 years.

References:

- ⇒ ***Okano A, Isley N, and Boger D. Peripheral modifications of [Ψ[CH2NH]Tpg4] vancomycin with added synergistic mechanisms of action provide durable and potent antibiotics. PNAS. 2017 May 30;114(26): 5052–5061.***
- ⇒ ***Phillips D. Modified Vancomycin Knocks Out Resistance: http://www.medscape.com/viewarticle/881354. Accessed June 2017.***

By: Amr Nowair, B.Sc.

FDA News

FDA Clears First Fixed-Dose Combination Treatment for Gout

On 18th August 2017, the Food and Drug Administration (FDA) has approved ***Duzallo*** , a fixed-dose oral combination of lesinurad [increases renal excretion of uric acid (UA)] and allopurinol [reduces the production of UA] or the treatment of hyperuricemia associated with gout in patients for whom target serum UA levels have not been achieved with allopurinol alone.

Once-daily ***Duzallo*** contains lesinurad 200 mg plus allopurinol 300 mg. ***Duzallo*** will also be available in a dose of lesinurad 200 mg plus allopurinol 200 mg. It is not recommended for the treatment of asymptomatic hyperuricemia.

The approval of ***Duzallo*** provides a new fixed-dose and dual-mechanism treatment option to help patients with uncontrolled gout achieve target serum uric acid levels. In clinical trials of adults with gout for whom target serum UA levels could not achieved with allopurinol alone, lesinurad in combination with allopurinol nearly doubled the number of patients in whom the serum UA target of <6 mg/dL at six months was achieved. It reduced the mean serum UA level to <6 mg/dL by one month and maintained that level through 12 months.

The most common adverse reactions in clinical trials were headache, influenza, increased levels of blood creatinine, and acid reflux. ***Duzallo*** has a boxed warning regarding the risk for acute renal failure. The drug should be taken in the morning with food and water, and patients should be advised to stay well hydrated and to drink about two litres of liquid a day when taking the drug.

References:

FDA Approves Duzallo: https://www.drugs.com/newdrugs/fda-approves-duzallo-lesinurad-allopurinol-hyperuricemia-patients-uncontrolled-gout-4580.html. Accessed August 2017.

By: Mai Mousa, Pharm D.

FDA Clears Non-invasive Device for Chronic Intractable Pain

Treatment of chronic pain costs an estimated $600 billion annually in the United States. The current standard of care for chronic pain includes "drug cocktails," such as corticosteroids, opiate pain relievers, and injections combined with treatments like physical therapy and counseling. Treatments can come with various short-term and long-term side effects.

The FDA has cleared a non-invasive neuromodulation device (*Stimpod NMS460*) for the relief of chronic intractable pain. The device applies a unique, patented pulsed radiofrequency (PRF) waveform to the affected area transcutaneously. It also incorporates nerve-locating technology.

Its stimulation probe is designed to direct the current to a particular nerve or region, such as a joint or muscle. It enables practitioners to evaluate the treatment progress of damaged nerves.

The device is focused on the symptomatic relief and management of chronic intractable pain, as well as adjunctive treatment in the management of postsurgical pain and post-traumatic acute pain problems, and as an adjunct for pain control due to rehabilitation. In addition to being non-invasive and non-drug-related, the device has zero side effects and a fast onset of effect at a fraction of the cost of comparable treatments.

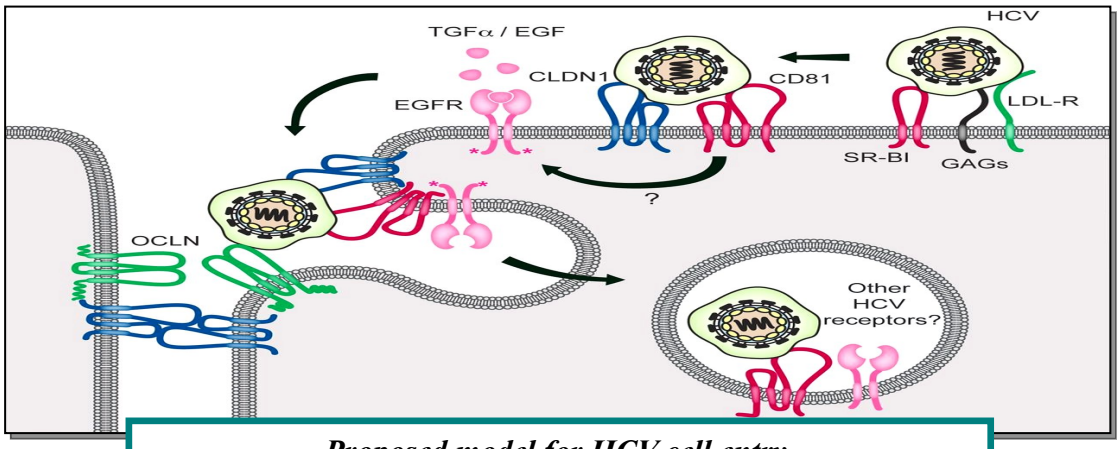
References:

Anderson P. FDA Clears Non-invasive Device for Intractable Pain: http://www.medscape.com/viewarticle/883653. Accessed September 2017.

By: Bassant Maher, B.Sc.

Aspirin Inhibits Hepatitis C Virus Entry by Downregulating Claudin-1

Hepatitis C virus (HCV) is a positive-sense single-stranded RNA virus of the flaviviridae family, infecting more than 170 million people globally. To date, however, no protective vaccine is available for HCV. The entry of HCV requires four receptors or co-receptors including SR-BI, CD81, claudin-1 and occludin.



Proposed model for HCV cell entry

Aspirin has previously been reported to inhibit hepatitis C virus (HCV) replication. *Yin P and Zhang L* aimed to investigate whether aspirin is involved in blocking HCV entry. They found that aspirin inhibits HCV entry in the HCV pseudoparticles (HCVpp) system by downregulating claudin-1. Claudin-1 is degraded by aspirin through the proteasome degradation pathway. As aspirin reduces claudin-1 levels, it can be deduced that it might inhibit entry of all genotypes of HCVpp. Previously aspirin was proposed as a novel therapeutic approach in combating established HCV infections by targeting COX-2. This study extend the anti-HCV effect of aspirin and suggest that aspirin may be beneficial in the earlier stages of infection or as a prophylactic approach to prevent HCV re-infection in patients with chronic hepatitis C (CHC) who are candidates for liver transplant.

References:

Yin P and Zhang L. Aspirin inhibits hepatitis C virus entry by downregulating claudin-1. J Viral Hepat. 2016 Jan;23(1):62-4.

By: Mai Mousa, Pharm D.

Inappropriate glove use among nursing assistants and spread of infections

Certified nursing assistants (CNAs) are often the main providers of care in long-term care facilities (LTCFs), with significant patient contact. The failure to change gloves is common among CNAs. Unfortunately, using gloves incorrectly leads to healthcare-associated infections (HAIs) in addition to spreading pathogens to patients and the environment.

The Centers for Disease Control and Prevention (CDC) recommends standard precautions for gloves use whish include:

1) All CNAs should wear personal protective equipment, especially gloves, to avoid contact with blood, secretions, excretions, or other potentially infectious materials that may contain pathogens.
2) All CNAs must change gloves as a standard precaution at the following glove change points during patient care:
   - When the gloves have touched blood or body fluids.
   - After the CNA completes a patient task.
   - After the gloves touch a potentially contaminated site.
   - In between patients.

New study was published on the September 2017 supports the findings of earlier studies that describe inappropriate glove use by healthcare personnel. Based on information from such studies, infection prevention staff and educators should develop training programs using adult learning principles and evidence-based instructional methods to improve glove use.

References:

⇒ *Inappropriate glove use among nursing assistants may be cause for spread of infections, study says: https://www.news-medical.net/news/20170908/Inappropriatec2a0glove-use-among-nursing-assistants-may-be-cause-for-spread-of-infections-study-says.aspx. Accessed September 2017.*

⇒ *Burdsall DP, Gardner SE, Cox T, et al. Exploring inappropriate certified nursing assistant glove use in long-term care. Am J Infect Control. 2017 Sep 1;45(9):940-945.*

By: Mai Mousa, Pharm D.

Egypt Upcoming Conferences

⇒ International Conferences on Medical and Health Science (ICMHS) will be held on 11th-12th November, 2017 in Cairo, Egypt.

⇒ Pan Arab Endodontic Conference (PAEC) will be held on 5th -8th December, 2017 at Dusit Thani LakeView Cairo, New Cairo, Egypt.

⇒ International Conference on Medical, Biological and Pharmaceutical Sciences (ICMBPS-17) will be held on 29th December, 2017 in Cairo, Egypt.

By: Bassant Maher, B.Sc.

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